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(71) Applicant *(for all designated States except US)*: AVENTIS PHARMA LIMITED [GB/GB]; Aventis House, 50 Kings Hill Avenue, West Malling, Kent ME19 4AH (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: CLARK, David, Edward [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). EASTWOOD, Paul, Robert [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). HARRIS, Neil, Victor [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). McCARTHY, Clive [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). MORLEY, Andrew, David [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB). PICKETT, Stephen, Dennis [GB/GB]; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB).

(74) Agent: CAFFIN, Lee; Aventis Pharma Limited, Rainham Road South, Dagenham, Essex RM10 7XS (GB).

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(54) Title: SUBSTITUTED BICYCLIC HETEROARYL COMPOUNDS AS INTEGRIN ANTAGONISTS

(57) Abstract

The invention is directed to physiologically active compounds of general formula (I) R^1Z^1–Het–L^1–Ar^1–L^2–Y wherein Het is an optionally substituted, saturated, partially saturated or fully unsaturated 8 to 10 membered bicyclic ring containing at least one heteroatom selected from O, S or N; R^1 is optionally substituted aryl, heteroaryl, alkyl, alkenyl, alkynyl, cycloalkyl or heterocycloalkyl; Z^1 represents a direct bond, an alkylene chain, NR^4, O or $S(O)_n$; L^1 is an a $-R^5-R^6-$ linkage where R^5 is alkylene, alkenylene or alkynylene and R^6 is a direct bond, cycloalkylene, heterocycloalkylene, arylene, heteroaryldiyl, $-C(=Z^3)-NR^4-$, $-NR^4-C(=Z^3)-$, $-Z^3-$, $-C(=O)-$, $-C(=NOR^4)-$, $-NR^4-$, $-NR^4-C(=Z^3)-NR^4-$, $-SO_2-NR^4-$, $-NR^4-SO_2-$, $-O-C(=O)-$, $-C(=O)-O-$, $-NR^4-C(=O)-O-$ or $-O-C(=O)-NR^4-$; L^2 is a direct bond; an optionally substituted alkylene, alkenylene, alkynylene, cycloalkenylene, cycloalkylene, heteroaryldiyl, heterocycloalkylene or arylene linkage; a $-[C(=O)-N(R^9)-C(R^4)(R^{10})]_p-$ linkage; a $-Z^4-R^{11}-$ linkage; a $-C(=O)-CH_2-C(=O)-$ linkage; a $-R^{11}-Z^4-R^{11}-$ linkage; or a $-L^3-L^4-L^5-$ linkage; and Y is carboxy or an acid bioisostere; and the corresponding N–oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds and their N–oxides and prodrugs. Such compounds have valuable pharmaceutical properties, in particular the ability to regulate the interaction of VCAM–1 and fibronectin with the integrin VLA–4 ($\alpha 4\beta 1$).